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KRISHNAN, GANAPATHY	
ART UNIT	**PAPER NUMBER**
1623	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/11/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	**Application No.** 10/679,194	**Applicant(s)** NILSSON, KURT
	Examiner Ganapathy Krishnan	**Art Unit** 1623

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 October 2006*.
2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.
3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26-73* is/are pending in the application.
4a) Of the above claim(s) *41 and 72* is/are withdrawn from consideration.
5)☐ Claim(s) _____ is/are allowed.
6)☒ Claim(s) *26-40,42-71 and 73* is/are rejected.
7)☐ Claim(s) _____ is/are objected to.
8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.
10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a)☒ All b)☐ Some * c)☐ None of:
1.☐ Certified copies of the priority documents have been received.
2.☒ Certified copies of the priority documents have been received in Application No. 08/666,542.
3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date *4/22/2004*.
4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election with traverse of Group 1, claims 26, 28-31, 36-37, 40, 42, 44-45 and 67-71 in the reply filed on 10/26/2006 is acknowledged. The traversal is on the ground(s) that Groups 1-3, 5 and 6 are all directed to producing a lactosamine compound with beta 1-4 linkages and do not relate to a different end product or end result and that Groups 1-3, 5 and 6 should be examined. Applicant's arguments are found to be persuasive. Groups 1-3, 5 and 6, Claims 26-40, 42-71 and 73 will be examined.

Claims 41 and 72 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 10/26/2006.

This application contains claims 41 and 72 drawn to an invention nonelected with traverse in Paper No. 10/26/2006. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

In the Election/Restriction mailed 9/26/2006 there were only six groups and not seven, due to a typographical error in the numbering.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 59 and 63 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the synthesis of the lactosamine in vitro, does not reasonably provide enablement for the synthesis of the lactosamine in vivo and conversion of the lactosamine to another desired product. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

A conclusion of lack of enablement means that, based on the evidence regarding each of the factors below, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation.

(A) The breadth of the claims
(B) The state of the prior art
(C) The level of one of ordinary skill
(D) The level of predictability in the art
(E) The amount of direction provided by the inventor
(F) The existence of working examples
(G) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The breadth of the claims

Claims 59 and 63 are drawn to a method of synthesis of a lactosamine containing compound in the presence of a glycosidase wherein the enzyme is used in vivo and adding a second enzyme to convert the galactosamine obtained to another desired product. Claim 59 is seen as drawn to the synthesis of the said lactosamine compound within the body based on the accepted meaning of the term in vivo. The terms second enzyme and desired product are broad and are seen to include any enzyme and any desired product.

The state of the prior art

The examiner notes that WO 89/09275 teaches similar synthesis in vitro and using specific enzymes. The art is silent regarding synthesis in vivo and the conversion of the lactosamine to any desired product.

The level of predictability in the art

There is not seen sufficient data to substantiate the claim that the enzyme could be used in vivo to synthesize the lactosamine or the use of a second enzyme to convert the lactosamine to a desired product. Enzymes are known to be specific. Any enzyme cannot be used for the said conversion. It is unpredictable that the use of an enzyme in vitro for a reaction will also work for the same in vivo. Several other factors come into play in vivo and it is highly unpredictable if the same reaction can be performed in vivo.

The amount of direction provided by the inventor

The instant specification is not seen to provide enough guidance that would allow a skilled artisan to extrapolate from the disclosure and the examples provided to enable the use of the said enzyme in vivo and adding a second enzyme to convert the galactosamine obtained to another desired product. The specification also fails to direct the skilled artisan in correlative prior art procedures which might provide the basis for the same.

The existence of working examples

The working examples set forth in the instant specification are drawn to the preparation of a lactosamine via the reaction of lactose and a few N-substituted glucosamines and a conversion of the lactosamine to a 2,3-slilylated lactosamine. Despite these examples there is little enabling disclosure for the synthesis of the lactosamine in vivo and conversion of the lactosamine to any other desired product. Applicant is therefore not entitled to all that is encompassed by the instant claim..

The quantity of experimentation needed to make or use the invention based on the content of the disclosure

Indeed, in view of the information set forth, the instant disclosure is not seen to be sufficient to enable the method as instantly claimed. One of ordinary skill in the art would have to carry out the process in order to determine if such a reaction could be made in vivo using the said enzyme and also determine which of the myriad of enzymes available would carry out the conversion to the myriad of desired products.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 26-40, 42-71 and 73 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 26 recites the broad recitation inorganic and/or organic group, and the claim also recites azido, acetyl, phthalimido which is the narrower statement of the range/limitation. Claim 26 also recites, "or another compound containing an inorganic and/or organic group bound to the 2-N". It is not clear what applicant intends by this recitation. Does applicant intend R'' to be a compound having the said groups on it attached to the nitrogen or an inorganic and/or organic group directly attached to the nitrogen? If applicant intends an inorganic and/or organic group attached to the nitrogen it is still a broad and narrow limitation since groups like azido, acetyl and phthalimido are inorganic and/or organic groups. This recitation is also seen in several other claims.

In claim 29 it is not clear what applicant means by a group containing an aliphatic and/or aromatic group. Does applicant intend a group that has an aliphatic group and/or aromatic group on it as a substituent? Or does applicant intend R and R' to be an aliphatic and/or aromatic group? The same recitation is also seen in claims 33 and 54.

In claim 38, step 3 is drawn to addition of a second enzyme to specifically remove glucose. Do applicants mean the glucopyranosamino group that is used in step 1b by the term glucose? Do applicants intend cleavage of an attached glucose unit by the recitation, "removes glucose"? It is not clear from where the glucose is removed.

The term "partially" in claim 46, step c is a relative term which renders the claim indefinite. The term "partially" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claim 63 recites another desired product. The recitation is broad and it is not clear what all products are encompassed by the said recitation. In the absence of the specific derivatizations to the chemical core claimed or distinct language to describe the structural modifications or the chemical names of the said product, the identity of the said product would be difficult to describe and the metes and bounds of said product applicant regards as the invention cannot be sufficiently determined because they have not been particularly pointed out or distinctly articulated in the claim.

Claim 66 is drawn to the synthesis of a substituted disaccharide comprising reacting lactose (a disaccharide composed of galactose attached to a glucose unit) with GlcNPhβSEt. Is the product a trisaccharide or is there a step wherein a glucose unit is removed from the resulting trisaccharide? Perusal of the specification indicates the removal of glucose unit but the claim is not clear regarding this step. Claim 71 is also drawn to a similar type of synthesis.

In claim 68 the structural formula recited at line 2, an oxygen atom is attached to the nitro group. The valence of this oxygen is not satisfied. Is there another atom or group attached to this oxygen? Or is the nitrophenyl glycoside of galactose structurally represented.

In claim 69 the structural formula recited at line 2, an oxygen atom is attached to the nitro group. The valence of this oxygen is not satisfied. Is there another atom or group attached to this oxygen? Or is the nitrophenyl glycoside of galactose structurally represented. The claim is also drawn to the synthesis of the structural formula at line 1 comprising a glucosamine unite with an azido group and a methoxy, but comprises the reaction of the nitrophenyl glycoside with another sugar which is a nitrophenyl galactose. It is not clear how the intended product can be obtained by the said combination of reactants. Are there additional steps involved?

Claim 73, step 3 is drawn to the use of alpha 2-3 sialyltransferase to obtain the corresponding alpha 2-3 silylated lactosamine. Does applicant mean obtaining the corresponding alpha 2-3 sialylated (i.e., transfer of a sialyl group) lactosamine?

Applicant is required to check all other claims in addition to the ones mentioned above for lack of clarity or indefiniteness in the recitations as above.

Claims that depend from a rejected base claim that is unclear/indefinite are also rendered unclear/indefinite and are rejected for the same reasons.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 26-40, 42-71 and 73 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-16 of U.S. Patent No. 6,653,109 ('109 patent).

Claims 26-40, 42-71 and 73 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-17 of U.S. Patent No. 6,077,695 ('695 patent).

Claims 26-40, 42-71 and 73 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-32 of U.S. Patent No. 6,183,994 ('994 patent).

Claims 26-40, 42-71 and 73 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-27 of U.S. Patent No. 5,856,143 ('143 patent).

Claims 26-40, 42-71 and 73 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-12 and 30-34 of U.S. Patent No. 5,532,147 patent).

Although the conflicting claims are not identical, they are not patentably distinct from each other because:

Instant claims 26-40, 42-71 and 73 are all drawn to the synthesis of a lactosamine compound with a beta 1-4 linkage comprising the reaction of a donor substance, which is galactose or a galactose ether and an acceptor, which is a glucopyranosamino compound in the presence of Bullera singularis or its disintegrated cells or an E.C. group 3.2 glycosidase.

The claims of the U.S. Patents listed above are all also drawn to a similar synthesis.

It would have been obvious to one of ordinary skill in the art at the time the invention was made that the instant claims are substantially overlapping with the claims of the U.S. patents listed above. The instant claims must recite limitations that are patentably distinct from those of the claims in the above patents.

One of ordinary skill in the art would be motivated to make the lactosamine containing compounds via the method as instantly claimed since the process steps, reagents and the conditions are the same and would know that the same method would work for the substrates as instantly claimed since the structural features of the instant starting materials are very close to those recited in the above U.S. patents and the site where the reaction takes place is the same.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 26-40, 42-71 and 73 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nilsson (WO 89/09275) in combination with Nilsson (Carbohydrate Research, 1987, 167, 95-103).

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Nilsson teaches a method of preparing oligosaccharides via the reaction of donor and acceptor substrates and a glycosidase (page 1, first paragraph; page 2, last paragraph). The enzymes are selected according to the final oligosaccharide to be synthesized. The enzymes (glycosidases) can be used in situ or after partial or complete purification and can be I the soluble form or be immobilized (page 4, last paragraph). Several glycosidases in the E.C. 3.2 groups are available for use (page 6, first paragraph). In Example 3 (page 8) Nilsson teaches the synthesis of the lactosamine containing compound Galβ1-4GlcNAc-OMe as instantly claimed that has a beta 1-4 linkage which is further sialylated using a second enzyme, alpha2-3sialyltransferase. The sue of CMP-Neu5Ac for the sialylation is also taught (page 9, example 6).

However, Nilsson does not teach an example wherein the glucosamine acceptor that has NR'' as azido and N-phthalimido and R''' as thioethyl and thiophenyl.

Nilsson (Carbohydrate Research), drawn to analogous disaccharides synthesis using glycosidase catalysis, teaches that the yields in such enzymatic synthesis are sufficiently high and the method using enzymes is simple (page 102, third paragraph).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the method as instantly claimed for the synthesis of a lactosamine containing compound since such a method using the substrates, enzymes and the process and conditions are all seen to be taught in the prior art.

One of ordinary skill in the art would be motivated to use the method as instantly claimed since it is simple to carry out, gives reasonably high yields and also has the potential of for changing regioselectivity of formation (Nilson, Carbohydrate Research).

It is well within the purview of one of ordinary skill in the art to use different substitutents on the substrate and substitute other enzymes in order to improve the yields over that reported in the prior art.

Conclusion

Claims 26-40, 42-71 and 73 are rejected

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ganapathy Krishnan whose telephone number is 571-272-0654. The examiner can normally be reached on 8.30am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia A. Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

GK

1/8/07

Shaojia Jiang
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